



where R¹⁰ and R¹¹ are independently selected from hydrogen or alkyl, particularly C₁₋₄ alkyl.

5 Preferably R² is carboxy or a pharmaceutically acceptable salt or ester thereof.

Suitable groups R³ include hydrogen, fluoro, chloro, bromo, iodo, methyl, cyano, trifluoromethyl, hydroxymethyl, alkoxyalkyl such as C₁₋₄alkoxymethyl, methoxy, benzyloxy, carboxyalkoxy such as carboxymethoxy, methylsulphanyl, methylsulphinyl, methylsulphonyl or carboxyC₃₋₆cycloalkyl, -(CHR²²)_r-NR²³R²⁴ (where r is 0-2, each R²² is independently

10 hydrogen or alkyl, in particular C₁₋₄ alkyl, R²³ and R²⁴ are independently selected from H and C₁₋₄alkyl or R²³ and R²⁴ together with the nitrogen to which they are attached form a 5 or 6 membered ring optionally containing one further heteroatom selected from O, N, S, S(O) or SO₂. Suitably R²³ and R²⁴ together form a heterocyclic ring such as morpholino or piperazinyl.

Other such groups R³ include optionally substituted aryl groups, such as optionally

15 substituted phenyl or naphthyl group. Suitable substituents for phenyl groups R³ include one or more groups selected from chlorine, fluorine, methyl, trifluoromethyl, trifluoromethoxy, amino, formyl, phenyl, methoxy, phenoxy or phenyl.

R³ may comprise a range of substituents as listed above, in particular, hydrogen or a small substituent group such as C₁₋₄alkyl in particular methyl, or trifluoromethyl, and is

20 preferably hydrogen.

Suitable optional substituents for the group R¹⁵, R¹⁶ and R¹⁷ as they appear in the definition of R⁴, include functional groups as hereinbefore defined, as well as aryl or heterocyclyl groups, either of which may themselves be substituted by one or more functional groups or further aryl or heterocyclyl groups.

25 Particular examples of substituents for groups R¹⁵, R¹⁶ and R¹⁷ include one or more groups selected from halo such as chloro; hydroxy; cyano; amino; mono- or di-alkylamino; C₁₋₄ alkoxy; carboxy; sulphonamido; CONH₂; alkylamido where the alkyl moiety is optionally substituted for example with a functional groups such as carboxy; morpholino;

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pyridyl; pyrimidinyl; phenyl optionally substituted by halo such as chloro, hydroxy, alkoxy such as methoxy, carbamoyl, acyl such as acetyl, or hydroxyalkyl where the alkyl group suitably includes at least two carbon atoms, such as hydroxyethyl. Other examples of substituents for phenyl groups R¹⁵ is alkanoylamino group such as methoxylamino.

- 5 Where R¹⁵, R¹⁶ and/or R¹⁷ is a heterocyclyl group, or where R¹⁶ and R¹⁷ together form an optionally substituted heterocyclic ring, these may be substituted by functional groups such as halo or hydroxy, or by alkyl groups such as methyl or ethyl, or alkenyl or alkynyl groups any of which may be substituted, for example with hydroxy, as well as with further heteroaryl groups such as pyridyl. Particular examples of heterocyclic groups R¹⁵, R¹⁶
10 and/or R¹⁷ are optionally substituted thiophenyl, optionally substituted imidazolyl, optionally substituted pyridyl.

Thus thiophenyl groups R¹⁵, R¹⁶ and/or R¹⁷ may comprise pyridyl-thiophenyl, whilst an example of a substituted imidazolyl group for R¹⁵, R¹⁶ and/or R¹⁷ is methylimidazolyl and halopyridyl in particular chloropyridyl is an example of a substituted pyridyl moiety for these groups.

Particular examples of R¹⁵ include alkyl in particular methyl optionally substituted by a functional groups or, in particular, a heterocyclyl group where the heterocyclyl group may be optionally substituted by a functional group such as halo or hydroxy or by an alkyl group such as methyl. Preferably, R¹⁵ is a substituted alkyl group. Where the substituent is a functional group, it is preferably a group of formula NR¹⁹R²⁰ where R¹⁹ and R²⁰ are as defined above. Thus examples of substituted alkyl groups R¹⁵ include morpholinomethyl or alkyl such as methyl substituted with a substituted alkyl amino group wherein the substituents include carboxy, alkanoyl, phenyl or alkyl sulphonyl.

Other examples of R¹⁵ are heterocycyl groups which are optionally substituted for example by alkyl such as methyl, functional groups such as chloro or heterocycyl groups such as pyridyl.

Particular examples of R¹⁶ and R¹⁷ are alkyl such as methyl.

X is CH_2 , or SO_2 , and is preferably CH_2 .

Suitable pharmaceutically acceptable salts of compounds of formula (I) include acid addition salts such as methanesulfonate, fumarate, hydrochloride, hydrobromide, citrate, maleate and salts formed with phosphoric and sulphuric acid. In another aspect suitable salts are base salts such as an alkali metal salt for example sodium, an alkaline earth metal salt for

example calcium or magnesium, an organic amine salt for example triethylamine, morpholine, *N*-methylpiperidine, *N*-ethylpiperidine, procaine, dibenzylamine, *N,N*-dibenzylethylamine or amino acids for example lysine. There may be more than one cation or anion depending on the number of charged functions and the valency of the cations or anions. A preferred

- 5 pharmaceutical acceptable salt is a sodium salt.

An *in vivo* hydrolysable ester of a compound of the formula (I) containing carboxy or hydroxy group is, for example, a pharmaceutically acceptable ester which is hydrolysed in the human or animal body to produce the parent acid or alcohol.

Suitable pharmaceutically acceptable esters for carboxy include alkyl esters, such as

- 10 C_{1-6} alkyl esters for example, ethyl esters, C_{1-6} alkoxymethyl esters for example methoxymethyl, C_{1-6} alkanoyloxymethyl esters for example pivaloyloxymethyl, phthalidyl esters, C_{1-8} cycloalkoxy-carbonyloxy C_{1-6} alkyl esters for example 1-cyclohexylcarbonyloxyethyl; 1,3-dioxolen-2-onylmethyl esters for example 5-methyl-1,3-dioxolen-2-onylmethyl; and C_{1-6} alkoxycarbonyloxyethyl esters for example
15 1-methoxycarbonyloxyethyl and may be formed at any carboxy group in the compounds of this invention.

Suitable pharmaceutically acceptable esters of compounds of formula (I) are *in vivo* hydrolysable ester of a compound of the formula (I) containing a hydroxy group includes inorganic esters such as phosphate esters and α -acyloxyalkyl ethers and related compounds

- 20 which as a result of the *in vivo* hydrolysis of the ester breakdown to give the parent hydroxy group. Examples of α -acyloxyalkyl ethers include acetoxymethoxy and 2,2-dimethylpropionyloxymethoxy. A selection of *in vivo* hydrolysable ester forming groups for hydroxy include alkanoyl, benzoyl, phenylacetyl and substituted benzoyl and phenylacetyl, alkoxycarbonyl (to give alkyl carbonate esters), dialkylcarbamoyl and
25 *N*-(dialkylaminoethyl)-*N*-alkylcarbamoyl (to give carbamates), dialkylaminoacetyl and carboxyacetyl.

Esters which are not *in vivo* hydrolysable are useful as intermediates in the production of the compounds of formula (I) and therefore these form a further aspect of the invention.

Thus examples of compounds of formula (I) include the following: